REMARKS

Applicants respectfully request entry of amendments to claims 12, 13, 16, and 18. Claims 1-11 were canceled by previous amendment. Claims 20-24 are withdrawn, without prejudice or disclaimer. Support for the amendments can be found throughout the specification, including paragraphs [0017], [0031], [0034]-[0037], [0040], [0047]-[0049], [0059], [0066], [0079], [0113], [0116], [0173], [0176], [0192], [0193], FIG. 1a, FIG. 2b, and the originally filed claims and, therefore, do not add new matter.

Applicants submit that pending claims 12-19 are in condition for allowance, and respectfully request that the claims as amended be entered.

Rejection Under 35 U.S.C. §112, Second Paragraph

Claims 12-19 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite.

Applicants traverse the rejection as it might apply to the amended claims for the reasons given below.

While not acquiescing to the reasoning offered in the Action, and to expedite prosecution toward allowance, Applicants have amended the claims such that the requisite nexus is clearly defined. For example, the recitation of element (c); i.e., hypermethylation of the 5' ALT promoter is correlated with p16 gene product truncation, and the detection of the truncated product indirectly indicates the presence of p16 gene methylation. As such, one of skill in the art would know the metes and bounds of the claims.

For these reasons, Applicants respectfully request that the rejection be withdrawn.

Rejection Under 35 U.S.C. §112, First Paragraph

Claims 16 and 17 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement.

Applicants traverse the rejection as it might apply to the amended claim, including the claim dependent therefrom, for the reasons given below.

The Office Action alleges, in pertinent part, that the claims are broadly drawn to detecting methylation in any [and all] neoplasm.

While not acquiescing to the reasoning offered in the Action, and to expedite prosecution toward allowance, Applicants have amended the claims such that only neoplastic cells which produce truncated p16, and produce a second amplification product corresponding to the full length p16 when such cells are treated with a demethylating agent, are embraced by the claims. Further, this element is expressly supported by the specification at paragraph [0193]:

> "The breast cancer cell line ZR75-1, which was partially methylated, expressed p16 message. To conform that this DNA methylation was essential for loss of transcription, the colon cancer cell lines RKO and SW480 was treated with the demethylating agent 5-deoxyazacytidine for 3 days. As in our studies of lung and bead and neck tumors, both colon cancer cell lines had detectable p16 mRNA after treatment with 5-deoxyazacytidine, suggesting that the aberrant DNA methylation is essential for maintaining transcriptional silencing."

Thus, the specification supports the notion that neoplastic cells, in which the truncated p16 gene product can be detected, can also produce the full length p16 gene product after contacting such cells with a demethylating agent (e.g., 5-deoxyazacytidine). As this reversal of truncation is ubiquitously associated with neoplastic cells that can be detected by the method as claimed (e.g., breast cancer, colon cancer, lung cancer, head and neck tumors), the amended claims no longer embraces any [and all] neoplasm as alleged in the Action.

Further, as this phenomenon was seen in breast cancer cell line ZR75-1, colon cancer cell lines RKO and SW480, lung, and bead and neck tumors (see also, Example 9), the specification provides sufficient guidance and working examples of the technique to identify such cells, and as the phenomenon directly correlates with 5' ALT promoter methylation via detection of differential production of full/truncated p16 gene products, one of skill in the art would predict that observation of the phenomenon in other neoplasms would be indicative 5' ALT dependent transcriptional silencing. Moreover, while the level of skill in this particular art is high, contrary to the position taken in the Action, there is sufficient correlative association for the phenomenon, where the skilled artisan would not have to exert inventive effort. Also, as the addition of a

demethylating agent to the reaction to observe the production of full length p16 requires no more than what is merely routine, such procedures do not rise to the level of undue experimentation.

Therefore, the claims are enabled because the specification provides appropriate guidance, working examples, and prediction of function based on observed properties of neoplastic cells such that one of skill in the art could practice the invention as claimed, in the absence of undue experimentation.

For these reasons, Applicants respectfully request that the rejection be withdrawn.

Rejections Under 35 U.S.C. §102

Claims 12-16 stand rejected under 35 U.S.C. §102(b), as allegedly being anticipated by Herbert et al.

Applicants traverse the rejection as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

The Office Action alleges, in pertinent part, that the cited reference teaches the elements as recited in the present claims. However, review of the Herbert et al. reference demonstrates that the primers as recited in the reference would not amplify the 5' ALT sequence.

The present claims expressly recite "amplifying the resulting extension products of step (a) [an extension product from exon 1 and exon 2 of p16] comprising contacting the extension products with a sense oligonucleotide which binds within and extends sequences from a 5' ALT promoter region" at step (b).

As stated in Hybritech Inc. v. Monoclonal Antibody, Inc., 231 U.S.P.Q. 81 (Fed. Cir. 1986), "It is axiomatic that for prior art to anticipate under 102 it has to meet every element of the claimed invention."

Therefore, because the cited reference fails to teach or suggest amplifying an extension products from exon 1 and exon 2 of p16 by "contacting the extension products with a sense oligonucleotide which binds within and extends sequences from a 5' ALT promoter region" the Herbert et al. reference does not anticipate the claimed invention.

Failure of the prior art to meet every element of the claimed invention does not meet the standard under §102. For these reasons, Applicants respectfully request that the rejection be withdrawn.

Claims 12 and 15-17 stand rejected under 35 U.S.C. §102(b), as allegedly being anticipated by Tulchinsky et al.

Applicants traverse the rejection as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

The Office Action alleges, in pertinent part, that the cited reference teaches the elements as recited in the present claims. However, review of the Tulchinsky et al. reference demonstrates that there is no amplification of the Mts1 gene using primers. Amplification in the section recited in the Action (i.e., Plasmid Constructions) is by cloning/subcloning. Further, Tulchinsky et al. only teach amplification using primers which are directed to the first **or** second exon, not to the 5' ALT. As such, the cited reference does not teach or suggest the elements of the present claims because the present claims expressly recite "amplifying the resulting extension products of step (a) [an extension product from exon 1 and exon 2 of p16] comprising contacting the extension products with a sense oligonucleotide which binds within and extends sequences from a 5' ALT promoter region"; i.e., amplification of the 5' ALT.

As stated in Hybritech Inc. v. Monoclonal Antibody, Inc., 231 U.S.P.Q. 81 (Fed. Cir. 1986), "It is axiomatic that for prior art to anticipate under 102 it has to meet every element of the claimed invention."

Therefore, because the cited reference fails to teach or suggest amplifying an extension products from exon 1 and exon 2 of p16 by "contacting the extension products with a sense oligonucleotide which binds within and extends sequences from a 5' ALT promoter region" the Tulchinsky et al. reference does not anticipate the claimed invention.

Failure of the prior art to meet every element of the claimed invention does not meet the standard under §102. For these reasons, Applicants respectfully request that the rejection be withdrawn.

Conclusion

Applicants submit that pending claims 12-19 are in condition for allowance. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this submission.

No fee is deemed necessary with the filing of this paper. However, the Commissioner is hereby authorized to charge any fees required by this submission, or credit any overpayments, to Deposit Account No. 07-1896 referencing the above-identified docket number. A duplicate copy the Transmittal Sheet is enclosed.

Respectfully submitted,

Date: December 6, 2006

Lisa A. Haile, J.D., Ph.D.
Registration No. 38,347
Telephone: (858) 677-1456
Facsimile: (858) 677-1465

DLA Piper US LLP
4365 Executive Drive, Suite 1100
San Diego, California 92121-2133
USPTO Customer Number 28213